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Rapid communication

Potentiation of anandamide hypotension by the transport inhibitor, AM404

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Abstract

The putative endogenous cannabinoid, anandamide (0.2–2 mg/kg i.v.), decreased systemic blood pressure dose-dependently in anesthesized guinea pigs. These effects were prevented by the CB1 cannabinoid receptor antagonist SR141716A [*N*-(piperidin-1-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-1*H*-pyrazole-3-carboxamide at the dose of 0.2 mg/kg i.v. The vasodepressor responses to anandamide were significantly potentiated and prolonged by a novel inhibitor of carrier-mediated anandamide transport, *N*-(4-hydroxyphenyl) arachidonylethanolamide (AM404) (10 mg/kg, i.v.). These results suggest that anandamide transport participates in terminating the vascular actions of anandamide.

Author Keywords: Cannabinoid; Anandamide; Vasculature

Index Terms: hypotension; drug transport; antihypertensive agent

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L9 ANSWER 32 OF 33 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:646587 CAPLUS
DOCUMENT NUMBER: 127:329390
TITLE: Potentiation of anandamide hypotension by the transport inhibitor, AM404
AUTHOR(S): Calignano, Antonio; La Rana, Giovanna; Beltramo, Massimiliano; Makriyannis, Alexandros; Piomelli, Daniele
CORPORATE SOURCE: Department of Experimental Pharmacology, University of Naples, Naples, 80123, Italy
SOURCE: European Journal of Pharmacology (1997), 337(1), R1-R2
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The putative endogenous cannabinoid, anandamide (0.2-2 mg/kg i.v.), decreased systemic blood pressure dose-dependently in anesthetized guinea pigs. These effects were prevented by the CB1 cannabinoid receptor antagonist SR141716A [N-(piperidin-1-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-1H-pyrazole-3-carboxamide.cntdot.HCl] at the dose of 0.2 mg/kg i.v. The vasodepressor responses to anandamide were significantly potentiated and prolonged by a novel inhibitor of carrier-mediated anandamide transport, N-(4-hydroxyphenyl) arachidonylethanolamide (AM404) (10 mg/kg, i.v.). These results suggest that anandamide transport participates in terminating the vascular actions of anandamide.

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25 ANSWER 1 OF 16 MEDLINE
ACCESSION NUMBER: 2002424217 MEDLINE
DOCUMENT NUMBER: 22166800 PubMed ID: 12177188
TITLE: Experimental parkinsonism alters endocannabinoid degradation: implications for striatal glutamatergic transmission.
AUTHOR: Gubellini Paolo; Picconi Barbara; Bari Monica; Battista Natalia; Calabresi Paolo; Centonze Diego; Bernardi Giorgio; Finazzi-Agro Alessandro; Maccarrone Mauro
CORPORATE SOURCE: Dipartimentos di Neuroscienze, Universita degli Studi di Roma Tor Vergata, 00133 Roma, Italy.. paolo.calabresi@uniroma2.it
SOURCE: JOURNAL OF NEUROSCIENCE, (2002 Aug 15) 22 (16) 6900-7. Journal code: 8102140. ISSN: 1529-2401.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200209
ENTRY DATE: Entered STN: 20020816
Last Updated on STN: 20020906
Entered Medline: 20020904

AB Cannabinoid receptors and their endogenous ligands have been recently identified in the brain as potent **inhibitors** of neurotransmitter release. Here we show that, in a rat model of Parkinson's disease induced by unilateral nigral lesion with 6-hydroxydopamine (6-OHDA), the striatal levels of anandamide, but not that of the other endocannabinoid 2-arachidonoylglycerol, were increased. Moreover, we observed a decreased activity of the anandamide membrane **transporter** (AMT) and of the anandamide hydrolase [fatty acid amide hydrolase (FAAH)], whereas the binding of anandamide to cannabinoid receptors was unaffected. Spontaneous glutamatergic activity recorded from striatal spiny neurons was higher in 6-OHDA-lesioned rats. **Inhibition** of AMT by N-(4-hydroxyphenyl)-arachidonoylamide (**AM**-404) or by VDM11, or stimulation of the cannabinoid CB1 receptor by HU-210 reduced glutamatergic spontaneous activity in both naive and 6-OHDA-lesioned animals to a similar extent. Conversely, the FAAH **inhibitors** phenylmethylsulfonyl fluoride and methyl-arachidonoyl fluorophosphonate were much more effective in 6-OHDA-lesioned animals. The present study shows that **inhibition** of anandamide hydrolysis might represent a possible target to decrease the abnormal cortical glutamatergic drive in Parkinson's disease.

L25 ANSWER 2 OF 16 MEDLINE
ACCESSION NUMBER: 2001668046 MEDLINE
DOCUMENT NUMBER: 21538477 PubMed ID: 11682448
TITLE: Anandamide-induced relaxation of sheep coronary arteries: the role of the vascular endothelium, arachidonic acid metabolites and potassium channels.
AUTHOR: Grainger J; Boachie-Ansah G
CORPORATE SOURCE: Institute of Pharmacy and Chemistry, University of Sunderland, Dale Building, Sunderland SR1 3SD.
SOURCE: BRITISH JOURNAL OF PHARMACOLOGY, (2001 Nov) 134 (5) 1003-12. Journal code: 7502536. ISSN: 0007-1188.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011121
Last Updated on STN: 20021217
Entered Medline: 20011207

09702165

AB 1. The effects of the endocannabinoid, anandamide, and its metabolically stable analogue, methanandamide, on induced tone were examined in sheep coronary artery rings in vitro. 2. In endothelium-intact rings precontracted to the thromboxane A(2) mimetic, U46619, anandamide (0.01 - 30 microM) induced slowly developing concentration-dependent relaxations (pEC(50) [negative log of EC(50)]=6.1+/-0.1; R(max) [maximum response]=81+/-4%). Endothelium denudation caused a 10 fold rightward shift of the anandamide concentration-relaxation curve without modifying R(max). Methanandamide was without effect on U46619-induced tone. 3. The anandamide-induced relaxation was unaffected by the cannabinoid receptor antagonist, SR 141716A (3 microM), the vanilloid receptor antagonist, capsazepine (3 and 10 microM) or the nitric oxide synthase **inhibitor**, L-NAME (100 microM). 4. The cyclo-oxygenase **inhibitor**, indomethacin (3 and 10 microM) and the anandamide amidohydrolase **inhibitor**, PMSF (70 and 200 microM), markedly attenuated the anandamide response. The anandamide **transport inhibitor**, **AM** 404 (10 and 30 microM), shifted the anandamide concentration-response curve to the right. 5. Precontraction of endothelium-intact rings with 25 mM KCl attenuated the anandamide-induced relaxations (R(max)=7+/-7%), as did K(+) channel blockade with tetraethylammonium (TEA; 3 microM) or iberiotoxin (100 nM). Blockade of small conductance, Ca(2+)-activated K(+) channels, delayed rectifier K(+) channels, K(ATP) channels or inward rectifier K(+) channels was without effect. 6. These data suggest that the relaxant effects of anandamide in sheep coronary arteries are mediated in part via the endothelium and result from the cellular uptake and conversion of anandamide to a vasodilatory prostanoid. This, in turn, causes vasorelaxation, in part, by opening potassium channels.

L25 ANSWER 3 OF 16 MEDLINE
ACCESSION NUMBER: 2001027409 MEDLINE
DOCUMENT NUMBER: 20493574 PubMed ID: 10913156
TITLE: Anandamide induces apoptosis in human cells via vanilloid receptors. Evidence for a protective role of cannabinoid receptors.
AUTHOR: Maccarrone M; Lorenzon T; Bari M; Melino G; Finazzi-Agro A
CORPORATE SOURCE: Department of Experimental Medicine and Biochemical Sciences, University of Rome Tor Vergata, Via di Tor Vergata 135, I-00133 Rome, Italy.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Oct 13) 275 (41) 31938-45.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001113

AB The endocannabinoid anandamide (AEA) is shown to induce apoptotic bodies formation and DNA fragmentation, hallmarks of programmed cell death, in human neuroblastoma CHP100 and lymphoma U937 cells. RNA and protein synthesis **inhibitors** like actinomycin D and cycloheximide reduced to one-fifth the number of apoptotic bodies induced by AEA, whereas the AEA **transporter inhibitor** AM404 or the AEA hydrolase **inhibitor** ATFMK significantly increased the number of dying cells. Furthermore, specific antagonists of cannabinoid or vanilloid receptors potentiated or **inhibited** cell death induced by AEA, respectively. Other endocannabinoids such as 2-arachidonoylglycerol, linoleoylethanolamide, oleoylethanolamide, and palmitoylethanolamide did not promote cell death under the same experimental conditions. The

formation of apoptotic bodies induced by AEA was paralleled by increases in intracellular calcium (3-fold over the controls), mitochondrial uncoupling (6-fold), and cytochrome c release (3-fold). The intracellular calcium chelator EGTA-**AM** reduced the number of apoptotic bodies to 40% of the controls, and electrotransferred anti-cytochrome c monoclonal antibodies fully prevented apoptosis induced by AEA. Moreover, 5-lipoxygenase **inhibitors** 5,8,11,14-eicosatetraynoic acid and MK886, cyclooxygenase **inhibitor** indomethacin, caspase-3 and caspase-9 **inhibitors** Z-DEVD-FMK and Z-LEHD-FMK, but not nitric oxide synthase **inhibitor** Nomega-nitro-l-arginine methyl ester, significantly reduced the cell death-inducing effect of AEA. The data presented indicate a protective role of cannabinoid receptors against apoptosis induced by AEA via vanilloid receptors.

L25 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:845822 CAPLUS
DOCUMENT NUMBER: 136:144957
TITLE: Anandamide-induced relaxation of sheep coronary arteries: the role of the vascular endothelium, arachidonic acid metabolites and potassium channels
AUTHOR(S): Grainger, J.; Boachie-Ansah, G.
CORPORATE SOURCE: Institute of Pharmacy and Chemistry, University of Sunderland, Sunderland, SR1 3SD, UK
SOURCE: British Journal of Pharmacology (2001), 134(5), 1003-1012
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 1 The effects of the endocannabinoid, anandamide, and its metabolically stable analog, methanandamide, on induced tone were examd. in sheep coronary artery rings in vitro. 2 In endothelium-intact rings precontracted to the thromboxane A2 mimetic, U46619, anandamide (0.01-30 .mu.M) induced slowly developing concn.-dependent relaxations (pEC50 [neg. log of EC50] = 6.1.+-.0.1; Rmax [max. response] = 81.+-.4%). Endothelium denudation caused a 10 fold rightward shift of the anandamide concn.-relaxation curve without modifying Rmax. Methanandamide was without effect on U46619-induced tone. 3 The anandamide-induced relaxation was unaffected by the cannabinoid receptor antagonist, SR 141716A (3 .mu.M), the vanilloid receptor antagonist, capsazepine (3 and 10 .mu.M) or the nitric oxide synthase **inhibitor**, L-NAME (100 .mu.M). 4 The cyclo-oxygenase **inhibitor**, indomethacin (3 and 10 .mu.M) and the anandamide amidohydrolase **inhibitor**, PMSF (70 and 200 .mu.M), markedly attenuated the anandamide response. The anandamide **transport inhibitor**, **AM** 404 (10 and 30 .mu.M), shifted the anandamide concn.-response curve to the right. 5 Precontraction of endothelium-intact rings with 25 mM KCl attenuated the anandamide-induced relaxations (Rmax = 7.+-.7%), as did K+ channel blockade with tetraethylammonium (TEA; 3 .mu.M) or iberiotoxin (100 nM). Blockade of small conductance, Ca2+-activated K+ channels, delayed rectifier K+ channels, KATP channels or inward rectifier K+ channels was without effect. 6 These data suggest that the relaxant effects of anandamide in sheep coronary arteries are mediated in part via the endothelium and result from the cellular uptake and conversion of anandamide to a vasodilatory prostanoid. This, in turn, causes vasorelaxation, in part, by opening potassium channels.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:494415 CAPLUS
DOCUMENT NUMBER: 135:283144

09702165

TITLE: Effects of topical anandamide-**transport inhibitors**, AM404 and olvanil, on intraocular pressure in normotensive rabbits
AUTHOR(S): Laine, Krista; Jarvinen, Tomi; Savinainen, Juha; Laitinen, Jarmo T.; Pate, David W.; Jarvinen, Kristiina
CORPORATE SOURCE: Department of Pharmaceutical Chemistry, University of Kuopio, Finland
SOURCE: Pharmaceutical Research (2001), 18(4), 494-499
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purpose of the study was to evaluate the effects of topically applied anandamide **transport inhibitors**, AM404 and olvanil, on the intraocular pressure (IOP) of normotensive rabbits. To det. if the ocular hypotension induced by topical anandamide (AEA) can be potentiated by co-administered AM404. Test compds., in either hydroxypropyl-.beta.-cyclodextrin (HP-.beta.-CD) or propylene glycol, were administered unilaterally onto rabbit eyes. To det. if AM404 affects the IOP-profile of AEA, AM404 was administered ocularly 15 min before topical AEA. Phenylmethylsulfonyl fluoride (PMSF) (24 mg/kg, s.c.) was given 30 min before AEA to prevent its catabolism. IOPs of the treated and untreated eyes were measured. The cannabinoid agonist activities of AM404 and olvanil were studied by using [35S]GTP.gamma.S autoradiog. Topical AM404 (62.5 .mu.g), in HP-.beta.-CD vehicle, decreased IOP significantly in treated eyes. AM404 (62.5 .mu.g) induced a significant IOP increase without subsequent decrease when given in propylene glycol vehicle. Olvanil (312.5 .mu.g) caused a significant IOP redn. without provoking an initial hypertensive phase. These compds. did not significantly affect the IOP of untreated eyes. Co-administered AM404 (125 .mu.g in HP-.beta.-CD) had no significant effect on the IOP profile of AEA (62.5 .mu.g). Ocular administration of AM404 or olvanil decreased IOP in rabbits, although AM404 can provoke an initial ocular hypertension and did not potentiate the IOP responses induced by exogenous AEA.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:402201 CAPLUS
DOCUMENT NUMBER: 135:239640
TITLE: Role of fatty acid amide hydrolase in the **transport** of the endogenous cannabinoid anandamide
AUTHOR(S): Day, Theresa A.; Rakhshan, Fariborz; Deutsch, Dale G.; Barker, Eric L.
CORPORATE SOURCE: Department of Medicinal Chemistry and Molecular Pharmacology, Purdue University School of Pharmacy and Pharmacal Sciences, West Lafayette, IN, USA
SOURCE: Molecular Pharmacology (2001), 59(6), 1369-1375
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A facilitated **transport** process that removes the endogenous cannabinoid anandamide from extracellular spaces has been identified. Once **transported** into the cytoplasm, fatty acid amide hydrolase (FAAH) is responsible for metabolizing the accumulated anandamide. The authors propose that FAAH contributes to anandamide uptake by creating and maintaining an inward concn. gradient for anandamide. To explore the role of FAAH in anandamide **transport**, the authors examd. anandamide

metab. and uptake in RBL-2H3 cells, which natively express FAAH, as well as wild-type HeLa cells that lack FAAH. RBL-2H3 and FAAH-transfected HeLa cells demonstrated a robust ability to metabolize anandamide compared with vector-transfected HeLa cells. This activity was reduced to that obsd. in wild-type HeLa cells upon the addn. of the FAAH **inhibitor** Me arachidonyl fluorophosphonate. Anandamide uptake was reduced in a dose-dependent manner by various FAAH **inhibitors** in both RBL-2H3 cells and wild-type HeLa cells. Anandamide uptake studies in wild-type HeLa cells showed that only FAAH **inhibitors** structurally similar to anandamide decreased anandamide uptake. Because there is no detectable FAAH activity in wild-type HeLa cells, these FAAH **inhibitors** are probably blocking uptake via actions on a plasma membrane **transport** protein. Phenylmethylsulfonyl fluoride, a FAAH **inhibitor** that is structurally unrelated to anandamide, **inhibited** anandamide uptake in RBL-2H3 cells and FAAH-transfected HeLa cells, but not in wild-type HeLa cells. Furthermore, expression of FAAH in HeLa cells increased maximal anandamide **transport** 2-fold compared with wild-type HeLa cells. These results suggest that FAAH facilitates anandamide uptake but is not solely required for **transport** to occur.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:322837 CAPLUS
DOCUMENT NUMBER: 135:132395
TITLE: Characterization of palmitoylethanolamide **transport** in mouse Neuro-2a neuroblastoma and rat RBL-2H3 basophilic leukaemia cells: comparison with anandamide
AUTHOR(S): Jacobsson, Stig O. P.; Fowler, Christopher J.
CORPORATE SOURCE: Department of Pharmacology and Clinical Neuroscience, Department of Odontology, Umea University, Umea, SE-901 87, Swed.
SOURCE: British Journal of Pharmacology (2001), 132(8), 1743-1754
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The endogenous cannabinoid receptor agonist anandamide (AEA) and the related compd. palmitoylethanolamide (PEA) are inactivated by **transport** into cells followed by metab. by fatty acid amide hydrolase (FAAH). The cellular uptake of AEA has been characterized in detail, whereas less is known about the properties of the PEA uptake, in particular in neuronal cells. In the present study, the pharmacol. and functional properties of PEA and AEA uptake have been investigated in mouse Neuro-2a neuroblastoma and, for comparison, in rat RBL-2H3 basophilic leukemia cells. Saturable uptake of PEA and AEA into both cell lines were demonstrated with apparent KM values of 28 .mu.M (PEA) and 10 .mu.M (AEA) in Neuro-2a cells, and 30 .mu.M (PEA) and 9.3 .mu.M (AEA) in RBL-2H3 cells. Both PEA and AEA uptake showed temp.-dependence but only the AEA uptake was sensitive to treatment with Pronase and phenylmethylsulfonyl fluoride. The AEA uptake was **inhibited** by AM404, 2-arachidonoylglycerol (2-AG), R1- and S1-methanandamide, arachidonic acid and olvanil with similar potencies for the two cell types. PEA, up to a concn. of 100 .mu.M, did not affect AEA uptake in either cell line. AEA, 2-AG, arachidonic acid, R1-methanandamide, .DELTA.9-THC, and cannabidiol **inhibited** PEA **transport** in both cell lines. The non-steroidal anti-inflammatory drug indomethacin **inhibited** the AEA uptake but had very weak effects on the uptake of PEA. From these data, it can be concluded that PEA is

transported in to cells both by passive diffusion and by a facilitated **transport** that is pharmacol. distinguishable from AEA uptake.

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:137736 CAPLUS
DOCUMENT NUMBER: 134:335978
TITLE: Structure-activity relationship for the endogenous cannabinoid, anandamide, and certain of its analogues at vanilloid receptors in transfected cells and vas deferens
AUTHOR(S): Ross, Ruth A.; Gibson, T. Michael; Brockie, Heather C.; Leslie, Mark; Pashmi, Ghazaleh; Craib, Susan J.; Di Marzo, Vincenzo; Pertwee, Roger G.
CORPORATE SOURCE: Department of Biomedical Sciences, Institute of Medical Sciences, University of Aberdeen, Aberdeen, AB25 2ZD, UK
SOURCE: British Journal of Pharmacology (2001), 132(3), 631-640
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This study was directed at exploring the structure-activity relation for anandamide and certain of its analogs at the rat VR1 receptor in transfected cells and at investigating the relative extent to which anandamide interacts with CB1 and vanilloid receptors in the mouse vas deferens. PKi values for displacement of [3H]-resiniferatoxin from membranes of rVR1 transfected CHO cells were significantly less for anandamide (5.78) than for its structural analogs N-(4-hydroxyphenyl)-arachidonylamide (AM404; 6.18) and N-(3-methoxy-4-hydroxy)benzyl-arachidonylamide (arvanil; 6.77). PEC50 values for stimulating 45Ca2+ uptake into rVR1 transfected CHO cells were significantly less for anandamide (5.80) than for AM404 (6.32) or arvanil (9.29). Arvanil was also significantly more potent than capsaicin (pEC50 = 7.37), a compd. with the same substituted benzyl polar head group as arvanil. In the mouse vas deferens, resiniferatoxin was 218 times more potent than capsaicin as an **inhibitor** of elec.-evoked contractions. Both drugs were antagonized to a similar extent by capsazepine (pKB = 6.93 and 7.18 resp.) but were not antagonized by SR141716A (1 .mu.M). Anandamide was less susceptible than capsaicin to antagonism by capsazepine (pKB = 6.02) and less susceptible to antagonism by SR141716A (pKB = 8.66) than methanandamide (pKB = 9.56). WIN55212 was antagonized by SR141716A (pKB = 9.02) but not by capsazepine (10 .mu.M). In conclusion, anandamide and certain of its analogs have affinity and efficacy at the rat VR1 receptor. In the mouse vas deferens, which seems to express vanilloid and CB1 receptors, both receptor types appear to contribute to anandamide-induced **inhibition** of evoked contractions.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:804901 CAPLUS
DOCUMENT NUMBER: 134:141665
TITLE: Elevated circulating levels of anandamide after administration of the **transport** **inhibitor**, AM404
AUTHOR(S): Giuffrida, A.; Rodriguez de Fonseca, F.; Nava, F.; Loubet-Lescoulie, P.; Piomelli, D.
CORPORATE SOURCE: Department of Pharmacology, University of California,

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Irvine, CA, 92697-4625, USA
SOURCE: European Journal of Pharmacology (2000), 408(2), 161-168
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The biol. actions of the endogenous cannabinoid anandamide are terminated by carrier-mediated **transport** into neurons and astrocytes, followed by enzymic hydrolysis. Anandamide **transport** is **inhibited** by the compd. N-(4-hydroxyphenyl)arachidonylamide (AM404). AM404 potentiates several responses elicited by administration of exogenous anandamide, suggesting that it may also protect endogenous anandamide from inactivation. To test this hypothesis, we studied the effects of AM404 on the plasma levels of anandamide using high-performance liq. chromatog./mass spectrometry (HPLC/MS). Systemic administration of AM404 (10 mg kg-1 i.p., i.p.) caused a gradual increase of anandamide in rat plasma, which was significantly different from untreated controls at 60 and 120 min after drug injection. In plasma, both AM404 and anandamide were assocd. with a plasma protein, which we identified as albumin by non-denaturing PAGE. AM404 (10 mg kg-1, i.p.) caused a time-dependent decrease of motor activity, which was reversed by the cannabinoid CB1 receptor antagonist N-(piperidin-1-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-1H-pyrazole-3-carboxamide.cntdot.hydrochloride (SR141716A, 0.5 mg kg-1, i.p). These results are consistent with the hypothesis that AM404 **inhibits** anandamide inactivation in vivo.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:753024 CAPLUS
DOCUMENT NUMBER: 133:348137
TITLE: Anandamide induces apoptosis in human cells via vanilloid receptors. Evidence for a protective role of cannabinoid receptors
AUTHOR(S): Maccarrone, Mauro; Lorenzon, Tatiana; Bari, Monica; Melino, Gerry; Finazzi-Agro, Alessandro
CORPORATE SOURCE: Department of Experimental Medicine and Biochemical Sciences, University of Rome Tor Vergata, Rome, I-00133, Italy
SOURCE: Journal of Biological Chemistry (2000), 275(41), 31938-31945
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The endocannabinoid anandamide (AEA) is shown to induce apoptotic bodies formation and DNA fragmentation, hallmarks of programmed cell death, in human neuroblastoma CHP100 and lymphoma U937 cells. RNA and protein synthesis **inhibitors** like actinomycin D and cycloheximide reduced to one-fifth the no. of apoptotic bodies induced by AEA, whereas the AEA **transporter inhibitor AM** 404 or the AEA hydrolase **inhibitor** ATFMK significantly increased the no. of dying cells. Furthermore, specific antagonists of cannabinoid or vanilloid receptors potentiated or **inhibited** cell death induced by AEA, resp. Other endocannabinoids such as 2-arachidonoylglycerol, linoleoylethanolamide, oleoylethanolamide, and palmitoylethanolamide did not promote cell death under the same exptl. conditions. The formation of apoptotic bodies induced by AEA was paralleled by increases in intracellular calcium (3-fold over the controls), mitochondrial uncoupling (6-fold), and cytochrome c release (3-fold). The intracellular calcium

chelator EGTA-**AM** reduced the no. of apoptotic bodies to 40% of the controls, and electrotransferred anti-cytochrome c monoclonal antibodies fully prevented apoptosis induced by AEA. Moreover, 5-lipoxygenase **inhibitors** 5,8,11,14-eicosatetraynoic acid and MK 886, cyclooxygenase **inhibitor** indomethacin, caspase-3 and caspase-9 **inhibitors** Z-DEVD-FMK and Z-LEHD-FMK, but not nitric oxide synthase **inhibitor** N.omega.-nitro-L-arginine Me ester, significantly reduced the cell death-inducing effect of AEA. The data presented indicate a protective role of cannabinoid receptors against apoptosis induced by AEA via vanilloid receptors.

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:719974 CAPLUS
DOCUMENT NUMBER: 134:50981
TITLE: Overlap between the ligand recognition properties of the anandamide **transporter** and the VR1 vanilloid receptor: **inhibitors** of anandamide uptake with negligible capsaicin-like activity
AUTHOR(S): De Petrocellis, L.; Bisogno, T.; Davis, J. B.; Pertwee, R. G.; Di Marzo, V.
CORPORATE SOURCE: Endocannabinoid Research Group, Istituto di Cibernetica, C.N.R., Arco Felice, Napoli, 80072, Italy
SOURCE: FEBS Letters (2000), 483(1), 52-56
CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Some synthetic agonists of the VR1 vanilloid (capsaicin) receptor also **inhibit** the facilitated **transport** into cells of the endogenous cannabinoid anandamide (arachidonoylethanolamide, AEA). Here we tested several AEA derivs. contg. various derivatized Ph groups or different alkyl chains as either **inhibitors** of the AEA membrane **transporter** (AMT) in intact cells or functional agonists of the VR1 vanilloid receptor in HEK cells transfected with the human VR1. We found that four known AMT **inhibitors**, AM404, arvanil, olvanil and linvanil, activate VR1 receptors at concns. 400-10000-fold lower than those necessary to **inhibit** the AMT. However, we also found three novel AEA derivs., named VDM11, VDM12 and VDM13, which **inhibit** the AMT as potently as AM404 but exhibit little or no agonist activity at hVR1. These compds. are weak **inhibitors** of AEA enzymic hydrolysis and poor CB1/CB2 receptor ligands. We show for the first time that, despite the overlap between the chem. moieties of AMT **inhibitors** and VR1 agonists, selective **inhibitors** of AEA uptake that do not activate VR1 (e.g. VDM11) can be developed.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:456872 CAPLUS
DOCUMENT NUMBER: 133:79360
TITLE: Preparation of pharmaceuticals containing anandamide **transport inhibitors** for glaucoma treatment
INVENTOR(S): Jarvinen, Tomi; Jarvinen, Kristiina; Urtti, Arto; Pate, David W.
PATENT ASSIGNEE(S): Finland
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

09702165

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000038671	A1	20000706	WO 1999-FI1069	19991222
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FI 9802793	A	20000624	FI 1998-2793	19981223

PRIORITY APPLN. INFO.: FI 1998-2793 A 19981223

AB The present invention concerns the use of anandamide **transport inhibitors**, esp. N-(4-hydroxyphenyl)arachidonylamide, for the topical treatment of ocular hypertension. The effect of topical administration of 0.25% N-(4-hydroxyphenyl)arachidonylamide (AM404) on the intraocular pressure (IOP) of normotensive pigmented rabbit was studied. Unilateral administration of 0.25% (m/v) AM404 significantly decreased IOP in the treated eyes in normotensive pigmented rabbits when compared to the control soln. AM404 showed a maximal IOP redn. of 4.5 mmHg 2 h after topical administration.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:345451 CAPLUS
DOCUMENT NUMBER: 133:84084
TITLE: The anandamide **transport inhibitor** AM404 activates vanilloid receptors
AUTHOR(S): Zygmunt, P. M.; Chuang, H.-h.; Movahed, P.; Julius, D.; Hogestatt, E. D.
CORPORATE SOURCE: Institute of Laboratory Medicine, Department of Clinical Pharmacology, Lund University, Lund, SE-221 85, Swed.
SOURCE: European Journal of Pharmacology (2000), 396(1), 39-42 CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The possibility that the anandamide **transport inhibitor** N-(4-hydroxyphenyl)-5,8,11,14-eicosatetraenamide (AM404), structurally similar to the vanilloid receptor agonists anandamide and capsaicin, may also activate vanilloid receptors and cause vasodilation was examd. AM404 evoked concn.-dependent relaxations in segments of rat isolated hepatic artery contracted with phenylephrine. Relaxations were abolished in prepns. pre-treated with capsaicin. The calcitonin-gene related peptide (CGRP) receptor antagonist CGRP-(8-37) also abolished relaxations. The vanilloid receptor antagonist capsazepine **inhibited** vasodilation by AM404 and blocked AM404-induced currents in patch-clamp expts. on Xenopus oocytes expressing the vanilloid subtype 1 receptor (VR1). In conclusion, AM404 activates native and cloned vanilloid receptors.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:296276 CAPLUS
DOCUMENT NUMBER: 133:53619

09702165

TITLE: Reversal of dopamine D2 receptor responses by an anandamide **transport inhibitor**
AUTHOR(S): Beltramo, Massimiliano; De Fonseca, Fernando Rodriguez; Navarro, Miguel; Calignano, Antonio; Gorriti, Miquel Angel; Grammatikopoulos, Georgios; Sadile, Adolfo G.; Giuffrida, Andrea; Piomelli, Daniele
CORPORATE SOURCE: The Neurosciences Institute, San Diego, CA, 92121, USA
SOURCE: Journal of Neuroscience (2000), 20(9), 3401-3407
CODEN: JNRSDS; ISSN: 0270-6474
PUBLISHER: Society for Neuroscience
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors characterized the pharmacol. properties of the anandamide **transport inhibitor** N-(4-hydroxyphenyl)-arachidonamide (AM404) in rats and investigated the effects of this drug on behavioral responses assocd. with activation of dopamine D2 family receptors. Rat brain slices accumulated [3H]anandamide via a high-affinity **transport** mechanism that was blocked by AM404. When administered alone in vivo, AM404 caused a mild and slow-developing hypokinesia that was significant 60 min after intracerebroventricular injection of the drug and was reversed by the CB1 cannabinoid receptor antagonist SR141716A. AM404 produced no significant catalepsy or analgesia, two typical effects of direct-acting cannabinoid agonists. However, AM404 prevented the stereotypic yawning produced by systemic administration of a low dose of apomorphine, an effect that was dose-dependent and blocked by SR141716A. Furthermore, AM404 reduced the stimulation of motor behaviors elicited by the selective D2 family receptor agonist quinpirole. Finally, AM404 reduced hyperactivity in juvenile spontaneously hypertensive rats, a putative model of attention deficit hyperactivity disorder. The results support a primary role of the endocannabinoid system in the regulation of psychomotor activity and point to anandamide **transport** as a potential target for neuropsychiatric medicines.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:698015 CAPLUS
DOCUMENT NUMBER: 130:76092
TITLE: Interactions between synthetic vanilloids and the endogenous cannabinoid system
AUTHOR(S): Di Marzo, Vincenzo; Bisogno, Tiziana; Melck, Dominique; Ross, Ruth; Brockie, Heather; Stevenson, Lesley; Pertwee, Roger; De Petrocellis, Luciano
CORPORATE SOURCE: Istituto per la Chimica di Molecole di Interesse Biologico, CNR, Arco Felice, 80072, Italy
SOURCE: FEBS Letters (1998), 436(3), 449-454
CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The chem. similarity between some synthetic agonists of vanilloid receptors, such as olvanil (N-vanillyl-cis-9-octadecenoamide), and the 'endocannabinoid' anandamide (arachidonoyl-ethanolamide, AEA), suggests possible interactions between the cannabinoid and vanilloid signalling systems. Here the authors report that olvanil is a stable and potent **inhibitor** of AEA facilitated **transport** into rat basophilic leukemia (RBL-2H3) cells. Olvanil blocked both the uptake and the hydrolysis of [14C]AEA by intact RBL-2H3 cells (IC50 = 9 .mu.M), while capsaicin and pseudocapsaicin (N-vanillyl-nonanamide) were much less active. Olvanil was more potent than previously reported **inhibitors** of AEA facilitated **transport**, i.e. phloretin

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(IC50 = 80 .mu.M), AM404 (12.9%, **inhibition** at 10 .mu.M) or oleoylethanolamide (27.5% **inhibition** at 10 .mu.M). Olvanil was a poor **inhibitor** of [14C]AEA hydrolysis by RBL-2H3 and N18TG2 cell membranes, suggesting that the **inhibitory** effect on [14C]AEA breakdown obsd. in intact cells was due to **inhibition** of [14C]AEA uptake. Olvanil was stable to enzymic hydrolysis, and (i) displaced the binding of high affinity cannabinoid receptor ligands to membrane prepns. from N18TG2 cells and guinea pig forebrain (Ki = 1.64-7.08 .mu.M), but not from cells expressing the CB2 cannabinoid receptor subtype; (ii) **inhibited** forskolin-induced cAMP formation in intact N18TG2 cells (IC50 = 1.60 .mu.M), this effect being reversed by the selective CB1 antagonist SR141716A. Pseudocapsaicin, but not capsaicin, also selectively bound to CB1 receptor-contg. membranes. These data suggest that some of the analgesic actions of olvanil may be due to its interactions with the endogenous cannabinoid system, and may lead to the design of a novel class of cannabimimetics with potential therapeutic applications as analgesics.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:646587 CAPLUS
DOCUMENT NUMBER: 127:329390
TITLE: Potentiation of anandamide hypotension by the **transport inhibitor**, AM404
AUTHOR(S): Calignano, Antonio; La Rana, Giovanna; Beltramo, Massimiliano; Makriyannis, Alexandros; Piomelli, Daniele
CORPORATE SOURCE: Department of Experimental Pharmacology, University of Naples, Naples, 80123, Italy
SOURCE: European Journal of Pharmacology (1997), 337(1), R1-R2
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The putative endogenous cannabinoid, anandamide (0.2-2 mg/kg i.v.), decreased systemic blood pressure dose-dependently in anesthetized guinea pigs. These effects were prevented by the CB1 cannabinoid receptor antagonist SR141716A [N-(piperidin-1-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-1H-pyrazole-3-carboxamide.cntdot.HCl] at the dose of 0.2 mg/kg i.v. The vasodepressor responses to anandamide were significantly potentiated and prolonged by a novel **inhibitor** of carrier-mediated anandamide **transport**, N-(4-hydroxyphenyl) arachidonylethanolamide (AM404) (10 mg/kg, i.v.). These results suggest that anandamide **transport** participates in terminating the vascular actions of anandamide.

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L16 ANSWER 15 OF 41 MEDLINE
ACCESSION NUMBER: 1998141027 MEDLINE
DOCUMENT NUMBER: 98141027 PubMed ID: 9537804
TITLE: **Inhibition** of intestinal motility by anandamide, an endogenous cannabinoid.
AUTHOR: Calignano A; La Rana G; Makriyannis A; Lin S Y; Beltramo M; Piomelli D
CORPORATE SOURCE: Department of Experimental Pharmacology, University of Naples, Italy.
SOURCE: EUROPEAN JOURNAL OF PHARMACOLOGY, (1997 Dec 11) 340 (2-3) R7-8.
Journal code: 1254354. ISSN: 0014-2999.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 19980416
Last Updated on STN: 19980416
Entered Medline: 19980403

AB The endogenous cannabinoid ligand anandamide (arachidonylethanolamide) **inhibited** the intestinal passage of a charcoal meal when administered s.c. in mice at doses ranging from 0.1 to 50 mg/kg. This effect was prevented by the cannabinoid CB1 receptor antagonist SR141716A [N-(piperidin-1-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-me thyl-1H-pyrazole-3-carboxamide x HCl] (1 mg/kg s.c.), but it was not affected by the **anandamide transport inhibitor**, N-(4-hydroxyphenyl) arachidonylethanolamide (AM404) (50 mg/kg, s.c.). The results indicate that anandamide modulates intestinal motility in mice by activating cannabinoid CB1 receptors. They also suggest that **anandamide transport**, which was previously shown to participate in terminating neural and vascular responses to anandamide, does not contribute to anandamide inactivation in intestinal tissue.

L16 ANSWER 16 OF 41 MEDLINE
ACCESSION NUMBER: 1998049257 MEDLINE
DOCUMENT NUMBER: 98049257 PubMed ID: 9389389
TITLE: Potentiation of anandamide hypotension by the transport **inhibitor**, AM404.
AUTHOR: Calignano A; La Rana G; Beltramo M; Makriyannis A; Piomelli D
CORPORATE SOURCE: Department of Experimental Pharmacology, University of Naples, Italy.
SOURCE: EUROPEAN JOURNAL OF PHARMACOLOGY, (1997 Oct 15) 337 (1) R1-2.
Journal code: 1254354. ISSN: 0014-2999.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980206
Last Updated on STN: 19980206
Entered Medline: 19980126

AB The putative endogenous cannabinoid, anandamide (0.2-2 mg/kg i.v.), decreased systemic blood pressure dose-dependently in anesthesized guinea pigs. These effects were prevented by the CB1 cannabinoid receptor antagonist SR141716A [N-(piperidin-1-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-me thyl-1H-pyrazole-3-carboxamide x HCl] at the dose of 0.2 mg/kg i.v. The vasodepressor responses to anandamide were

significantly potentiated and prolonged by a novel **inhibitor** of carrier-mediated **anandamide transport**, N-(4-hydroxyphenyl) arachidonylethanolamide (AM404) (10 mg/kg, i.v.). These results suggest that **anandamide transport** participates in terminating the vascular actions of anandamide.

L16 ANSWER 17 OF 41 MEDLINE

ACCESSION NUMBER: 97407976 MEDLINE
DOCUMENT NUMBER: 97407976 PubMed ID: 9262477
TITLE: Functional role of high-affinity **anandamide transport**, as revealed by selective **inhibition**.
AUTHOR: Beltramo M; Stella N; Calignano A; Lin S Y; Makriyannis A; Piomelli D
CORPORATE SOURCE: The Neurosciences Institute, 10640 J. J. Hopkins Drive, San Diego, CA 92121, USA.
SOURCE: SCIENCE, (1997 Aug 22) 277 (5329) 1094-7.
Journal code: 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19970922
Last Updated on STN: 19970922
Entered Medline: 19970911

AB Anandamide, an endogenous ligand for central cannabinoid receptors, is released from neurons on depolarization and rapidly inactivated. Anandamide inactivation is not completely understood, but it may occur by transport into cells or by enzymatic hydrolysis. The compound N-(4-hydroxyphenyl)arachidonylamide (AM404) was shown to **inhibit** high-affinity anandamide accumulation in rat neurons and astrocytes in vitro, an indication that this accumulation resulted from carrier-mediated transport. Although AM404 did not activate cannabinoid receptors or **inhibit** anandamide hydrolysis, it enhanced receptor-mediated anandamide responses in vitro and in vivo. The data indicate that carrier-mediated transport may be essential for termination of the biological effects of anandamide, and may represent a potential drug target.

L16 ANSWER 38 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:808015 CAPLUS
DOCUMENT NUMBER: 128:136686
TITLE: **Inhibition** of intestinal motility by anandamide, an endogenous cannabinoid
AUTHOR(S): Calignano, Antonio; La Rana, Giovanna; Makriyannis, Alexandros; Lin, Sun Y.; Beltramo, Massimiliano; Piomelli, Daniele
CORPORATE SOURCE: Department of Experimental Pharmacology, University of Naples, Naples 80123, Italy
SOURCE: European Journal of Pharmacology (1997), 340(2/3), R7-R8
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The endogenous cannabinoid ligand anandamide (arachidonylethanolamide) **inhibited** the intestinal passage of a charcoal meal when administered s.c. in mice at doses ranging from 0.1 to 50 mg/kg. This effect was prevented by the cannabinoid CB1 receptor antagonist SR141716A [N-(piperidin-1-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-1H-pyrazole-3-carboxamide.cntdot.HCl] (1 mg/kg s.c.), but it was not affected by the **anandamide transport inhibitor,** N-(4-hydroxyphenyl) arachidonylethanolamide (AM404) (50 mg/kg, s.c.). The results indicate that anandamide modulates intestinal motility in mice by activating cannabinoid CB1 receptors. They also suggest that **anandamide transport,** which was previously shown to participate in terminating neural and vascular responses to anandamide, does not contribute to anandamide inactivation in intestinal tissue.

L16 ANSWER 39 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:646587 CAPLUS
DOCUMENT NUMBER: 127:329390
TITLE: Potentiation of anandamide hypotension by the transport **inhibitor,** AM404
AUTHOR(S): Calignano, Antonio; La Rana, Giovanna; Beltramo, Massimiliano; Makriyannis, Alexandros; Piomelli, Daniele
CORPORATE SOURCE: Department of Experimental Pharmacology, University of Naples, Naples, 80123, Italy
SOURCE: European Journal of Pharmacology (1997), 337(1), R1-R2
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The putative endogenous cannabinoid, anandamide (0.2-2 mg/kg i.v.), decreased systemic blood pressure dose-dependently in anesthetized guinea pigs. These effects were prevented by the CB1 cannabinoid receptor antagonist SR141716A [N-(piperidin-1-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-1H-pyrazole-3-carboxamide.cntdot.HCl] at the dose of 0.2 mg/kg i.v. The vasodepressor responses to anandamide were significantly potentiated and prolonged by a novel **inhibitor** of carrier-mediated **anandamide transport,** N-(4-hydroxyphenyl) arachidonylethanolamide (AM404) (10 mg/kg, i.v.). These results suggest that **anandamide transport** participates in terminating the vascular actions of anandamide.

L16 ANSWER 40 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:550217 CAPLUS

09702165

DOCUMENT NUMBER: 127:246072
TITLE: Functional role of high-affinity **anandamide transport**, as revealed by selective **inhibition**
AUTHOR(S): Beltramo, M.; Stella, N.; Calignano, A.; Lin, S. Y.; Makriyannis, A.; Piomelli, D.
CORPORATE SOURCE: The Neurosciences Inst., San Diego, CA, 92121, USA
SOURCE: Science (Washington, D. C.) (1997), 277(5329), 1094-1097
CODEN: SCIEAS; ISSN: 0036-8075
PUBLISHER: American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Anandamide, an endogenous ligand for central cannabinoid receptors, is released from neurons on depolarization and rapidly inactivated. Anandamide inactivation is not completely understood, but it may occur by transport into cells or by enzymic hydrolysis. The compd. N-(4-hydroxyphenyl)arachidonylamide (AM404) was shown to **inhibit** high-affinity anandamide accumulation in rat neurons and astrocytes in vitro, an indication that this accumulation resulted form carrier-mediated transport. Although AM404 did not activate cannabinoid receptors or **inhibit** anandamide hydrolysis, it enhanced receptor-mediated anandamide responses in vitro and in vivo. The data indicate that carrier-mediated transport may be essential for termination of the biol. effects of anandamide, and may represent a potential drug target.

L16 ANSWER 41 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:495779 CAPLUS
DOCUMENT NUMBER: 127:188622
TITLE: Accumulation of N-arachidonoylethanolamine (anandamide) into cerebellar granule cells occurs via facilitated diffusion
AUTHOR(S): Hillard, Cecilia J.; Edgemond, William S.; Jarrahian, Abbas; Campbell, William B.
CORPORATE SOURCE: Department of Pharmacology and Toxicology, Medical College of Wisconsin, Milwaukee, WI, 53226, USA
SOURCE: Journal of Neurochemistry (1997), 69(2), 631-638
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Lippincott-Raven
DOCUMENT TYPE: Journal
LANGUAGE: English

AB N-Arachidonoylethanolamine (anandamide, AEA) is a putative endogenous ligand of the cannabinoid receptor. Intact cerebellar granule neurons in primary culture rapidly accumulate AEA. [3H]AEA accumulation by cerebellar granule cells is dependent on incubation time (t1/2 of 2.6 .+-. 0.8 min at 37.degree.C) and temp. The accumulation of AEA is saturable and has an apparent Km of 41 .+-. 15 .mu.M and a Vmax of 0.61 .+-. 0.04 nmol/min/106 cells. [3H]AEA,accumulation by cerebellar granule cells is significantly reduced by 200 .mu.M phloretin (57.4 .+-. 4% of control) in a noncompetitive manner. [3H]AEA accumulation is not **inhibited** by either ouabain or removal of extracellular sodium. [3H]AEA accumulation is fairly selective for AEA among other naturally occurring N-acylethanolamines; only N-oleoylethanolamine significantly **inhibited** [3H]AEA accumulation at a concn. of 10 .mu.M. The ethanolamides of palmitic acid and linolenic acid were inactive at 10 .mu.M. N-Arachidonoylbenzylamine and N-arachidonoylpropylamine, but not arachidonic acid, 15-hydroxy-AEA, or 12-hydroxy-AEA, compete for AEA accumulation. When cells are preloaded with [3H]AEA, temp.-dependent efflux occurs with a half-life of 1.9 .+-. 1.0 min. Phloretin does not **inhibit** [3H]AEA efflux from cells. These results suggest that AEA

is accumulated by cerebellar granule cells by a protein-mediated transport process that has the characteristics of facilitated diffusion.

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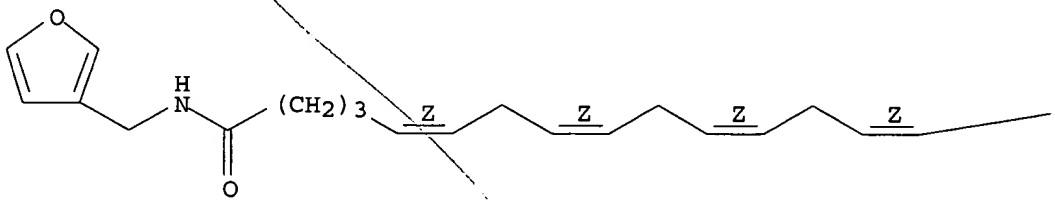
L16 ANSWER 41 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:495779 CAPLUS
DOCUMENT NUMBER: 127:188622
TITLE: Accumulation of N-arachidonoylethanolamine (anandamide) into cerebellar granule cells occurs via facilitated diffusion
AUTHOR(S): Hillard, Cecilia J.; Edgemond, William S.; Jarrahian, Abbas; Campbell, William B.
CORPORATE SOURCE: Department of Pharmacology and Toxicology, Medical College of Wisconsin, Milwaukee, WI, 53226, USA
SOURCE: Journal of Neurochemistry (1997), 69(2), 631-638
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Lippincott-Raven
DOCUMENT TYPE: Journal
LANGUAGE: English

AB N-Arachidonoylethanolamine (anandamide, AEA) is a putative endogenous ligand of the cannabinoid receptor. Intact cerebellar granule neurons in primary culture rapidly accumulate AEA. [3H]AEA accumulation by cerebellar granule cells is dependent on incubation time (t1/2 of 2.6 .+-. 0.8 min at 37.degree.C) and temp. The accumulation of AEA is saturable and has an apparent Km of 41 .+-. 15 .mu.M and a Vmax of 0.61 .+-. 0.04 nmol/min/106 cells. [3H]AEA,accumulation by cerebellar granule cells is significantly reduced by 200 .mu.M phloretin (57.4 .+-. 4% of control) in a noncompetitive manner. [3H]AEA accumulation is not **inhibited** by either ouabain or removal of extracellular sodium. [3H]AEA accumulation is fairly selective for AEA among other naturally occurring N-acylethanolamines; only N-oleoylethanolamine significantly **inhibited** [3H]AEA accumulation at a concn. of 10 .mu.M. The ethanolamides of palmitic acid and linolenic acid were inactive at 10 .mu.M. N-Arachidonoylbenzylamine and N-arachidonoylpropylamine, but not arachidonic acid, 15-hydroxy-AEA, or 12-hydroxy-AEA, compete for AEA accumulation. When cells are preloaded with [3H]AEA, temp.-dependent efflux occurs with a half-life of 1.9 .+-. 1.0 min. Phloretin does not **inhibit** [3H]AEA efflux from cells. These results suggest that AEA is accumulated by cerebellar granule cells by a protein-mediated transport process that has the characteristics of facilitated diffusion.

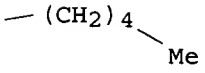
19 ANSWER 1 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
RN 390824-20-1 REGISTRY
CN 5,8,11,14-Eicosatetraenamide, N-(3-furanylmethyl)-, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **N-(Fur-3-ylmethyl)arachidonamide**
CN UCM 707
FS STEREOSEARCH
MF C25 H37 N O2
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, CASREACT, RTECS*, SYNTHLINE, TOXCENTER
(*File contains numerically searchable property data)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

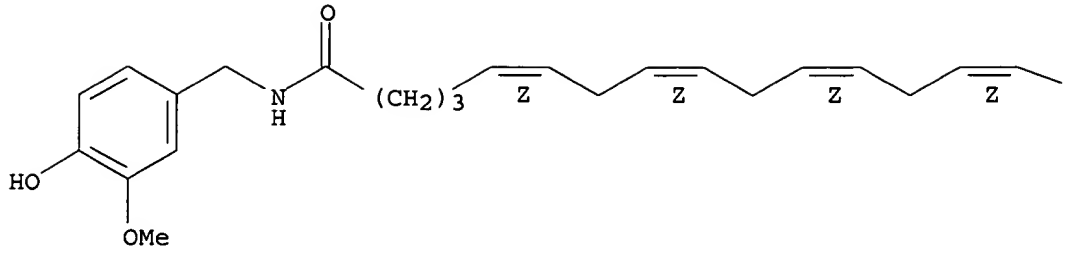


7 REFERENCES IN FILE CA (1907 TO DATE)
7 REFERENCES IN FILE CAPLUS (1907 TO DATE)

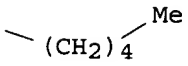
L19 ANSWER 2 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
RN 128007-31-8 REGISTRY
CN 5,8,11,14-Eicosatetraenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 5,8,11,14-Eicosatetraenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (all-Z)-
OTHER NAMES:
CN Arvanil
CN **N-Vanillylarachidonamide**
FS STEREOSEARCH
MF C28 H41 N O3
SR CA
LC STN Files: BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CHEMCATS, CSCHEM, EMBASE, RTECS*, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



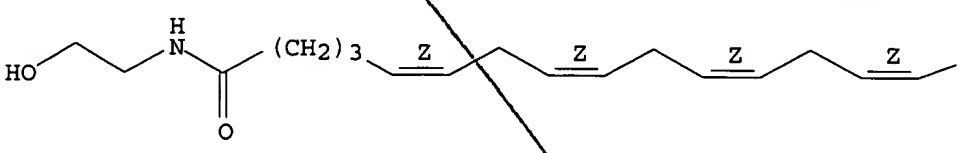
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

18 REFERENCES IN FILE CA (1907 TO DATE)
18 REFERENCES IN FILE CAPLUS (1907 TO DATE)

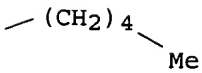
L19 ANSWER 3 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
RN 94421-68-8 REGISTRY
CN 5,8,11,14-Eicosatetraenamide, N-(2-hydroxyethyl)-, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 5,8,11,14-Eicosatetraenamide, N-(2-hydroxyethyl)-, (all-Z)-
OTHER NAMES:
CN Anandamide
CN Arachidonylethanolamide
CN **N-(2-Hydroxyethyl)arachidonamide**
CN N-(2-Hydroxyethyl)arachidonylamide
CN N-Arachidonylethanolamine
FS STEREOSEARCH
MF C22 H37 N O2
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CEN, CHEMCATS, CIN, CSCHEM, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, RTECS*, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

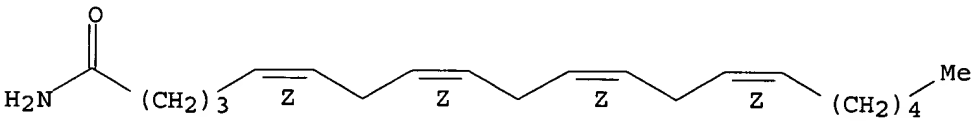


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

839 REFERENCES IN FILE CA (1907 TO DATE)
23 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
842 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L19 ANSWER 4 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
RN 85146-53-8 REGISTRY
CN 5,8,11,14-Eicosatetraenamide, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 5,8,11,14-Eicosatetraenamide, (all-Z)-
OTHER NAMES:
CN **Arachidonamide**
CN L 737993
FS STEREOSEARCH
MF C20 H33 N O
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAPLUS, CHEMCATS, MSDS-OHS, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Double bond geometry as shown.



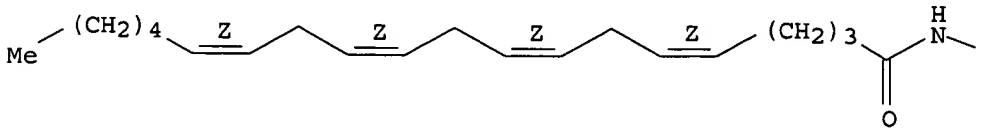
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

28 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
28 REFERENCES IN FILE CAPLUS (1907 TO DATE)

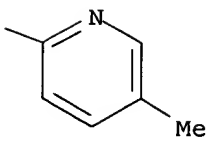
L19 ANSWER 5 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
RN 28273-78-1 REGISTRY
CN **Arachidonamide, N-(5-methyl-2-pyridyl)- (7CI, 8CI)** (CA INDEX NAME)
FS STEREOSEARCH
MF C26 H38 N2 O
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, TOXCENTER
(*File contains numerically searchable property data)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



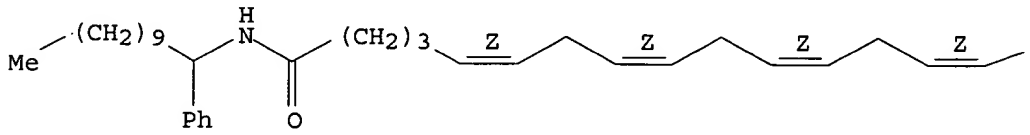
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

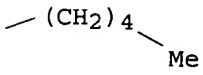
L19 ANSWER 6 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
RN 25275-82-5 REGISTRY
CN **Arachidonamide, N-(1-phenylundecyl)- (8CI)** (CA INDEX NAME)
FS STEREOSEARCH
MF C37 H59 N O
LC STN Files: BEILSTEIN*, CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, USPATFULL
(*File contains numerically searchable property data)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



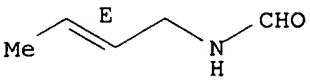
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=>

RN 62398-14-5 REGISTRY
CN Formamide, N-2-butenyl-, (E)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C5 H9 N O
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)

Double bond geometry as shown.



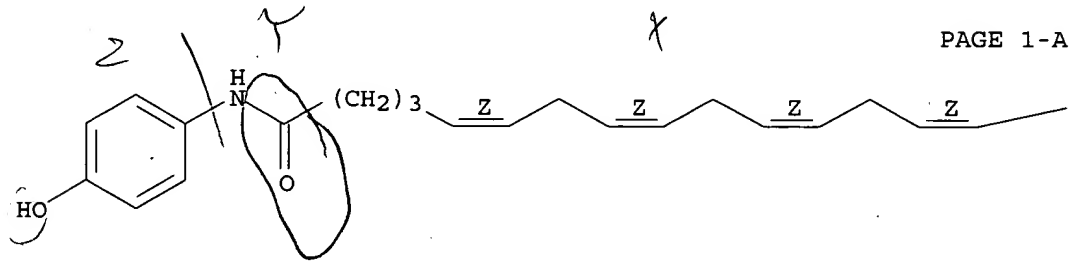
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

09702165

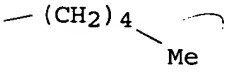
L5 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN 183718-77-6 REGISTRY
CN 5,8,11,14-Eicosatetraenamide, N-(4-hydroxyphenyl)-, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 5,8,11,14-Eicosatetraenamide, N-(4-hydroxyphenyl)-, (all-Z)-
OTHER NAMES:
CN **AM 404**
FS STEREOSEARCH
DR 198022-70-7
MF C26 H37 N O2
SR CA
LC STN Files: BIOSIS, BIOTECHNO, CA, CAPLUS, CHEMCATS, CSCHEM, EMBASE, TOXCENTER, USPATFULL

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

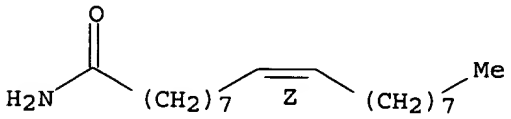


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

33 REFERENCES IN FILE CA (1962 TO DATE)
33 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 301-02-0 REGISTRY
CN 9-Octadecenamide, (9Z)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 9-Octadecenamide, (Z)-
CN **Oleamide (6CI, 8CI)**
OTHER NAMES:
CN (Z)-9-Octadecenamide
CN 9-cis-Oleamide
CN Adogen 73
CN Alflow 10E
CN Alflow E 10
CN Amide O
CN Amide O-N
CN Armoslip CP
CN Armoslip CP Flake
CN Armoslip CP-P
CN cis-9-10-Octadecenoamide
CN Crodamide O
CN Crodamide OR
CN Crodamide VR
CN Denon SL 1
CN Diamid O
CN Diamid O 200
CN Diamide O 200
CN Kemamide O
CN Kemamide U
CN O 200
CN Oleic acid amide
CN Oleylamide
CN Petrac Slip-eze
CN PP 5926
CN Slip-eze
CN Unislip 1757
CN Unislip 4407
FS STEREOSEARCH
DR 94554-98-0, 65862-65-9, 69899-60-1, 181057-55-6
MF C18 H35 N O
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DETHERM*, EMBASE, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, NIOSHTIC, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

Double bond geometry as shown.



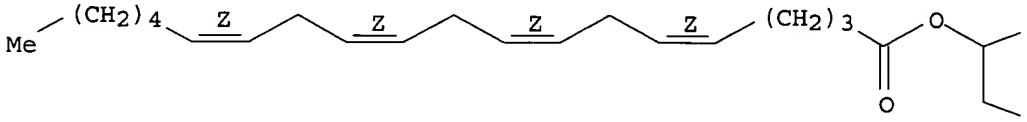
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1295 REFERENCES IN FILE CA (1907 TO DATE)
43 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1298 REFERENCES IN FILE CAPLUS (1907 TO DATE)
44 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

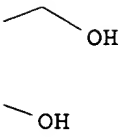
L3 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN
RN 53847-30-6 REGISTRY
CN 5,8,11,14-Eicosatetraenoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 5,8,11,14-Eicosatetraenoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester, (all-Z)-
OTHER NAMES:
CN **2-Arachidonylglycerol**
CN 2-Monoarachidonoylglycerol
FS STEREOSEARCH
DR 75656-17-6
MF C23 H38 O4
LC STN Files: AGRICOLA, ANABSTR, BIOSIS, CA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, CSCHEM, MEDLINE, RTECS*, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

221 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
225 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L8 ANSWER 27 OF 28 USPATFULL on STN

ACCESSION NUMBER:	2002:34468 USPATFULL
TITLE:	Control of pain with endogenous cannabinoids
INVENTOR(S):	Calignano, Antonio, Naples, ITALY La Rana, Giovanna, Naples, ITALY Guiffrida, Andrea, Laguna Beach, CA, United States Piomelli, Daniele, Irvine, CA, United States
PATENT ASSIGNEE(S):	Neurosciences Research Foundation, Inc., San Diego, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6348498	B1	20020219	
APPLICATION INFO.:	US 1999-322843		19990528	(9)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1998-87289P	19980529	(60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Krass, Frederick
LEGAL REPRESENTATIVE:	McDermott, Will & Emery
NUMBER OF CLAIMS:	10
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	13 Drawing Figure(s); 6 Drawing Page(s)
LINE COUNT:	679

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel pharmaceutical therapeutic compositions and methods for using same for the treatment of pain experienced by an individual are provided. The compositions contain at least one member selected from among anandamide and palmitylethanolamide.

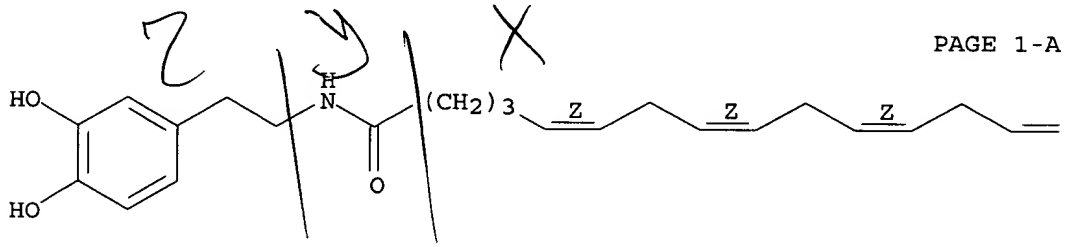
—Me

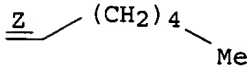
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

16 REFERENCES IN FILE CA (1907 TO DATE)
16 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L28 ANSWER 24 OF 51 REGISTRY COPYRIGHT 2004 ACS on STN
RN 199875-69-9 REGISTRY
CN 5,8,11,14-Eicosatetraenamide, N-[2-(3,4-dihydroxyphenyl)ethyl]-, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 5,8,11,14-Eicosatetraenamide, N-[2-(3,4-dihydroxyphenyl)ethyl]-, (all-Z)-
OTHER NAMES:
CN **N-Arachidonyldopamine**
FS STEREOSEARCH
MF C28 H41 N O3
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, CASREACT, CHEMCATS, TOXCENTER

Double bond geometry as shown.

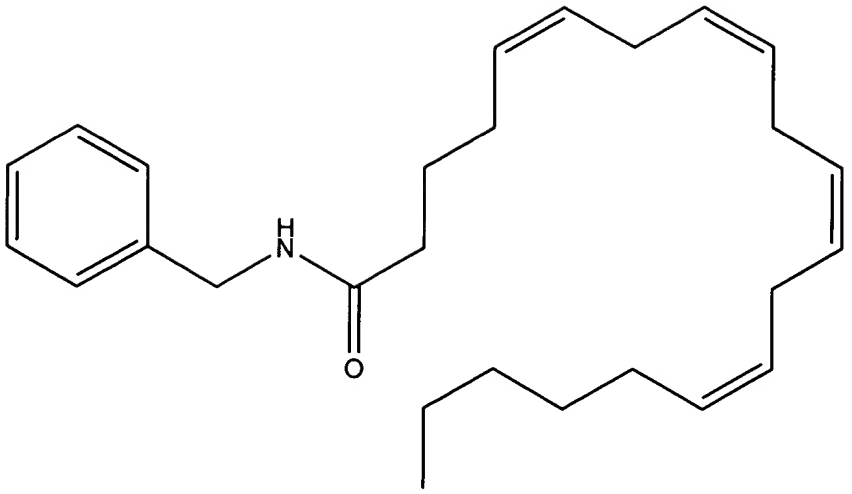




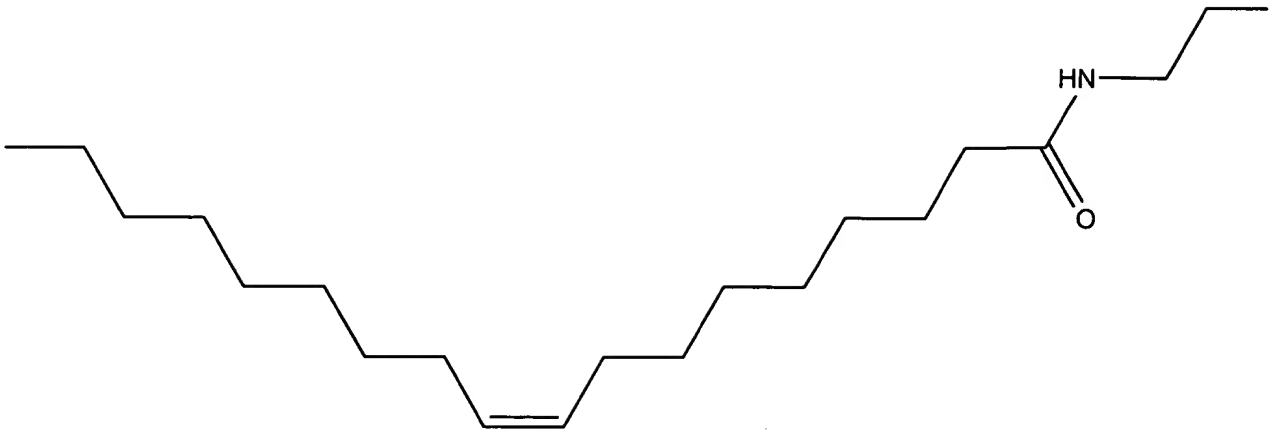
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

12 REFERENCES IN FILE CA (1907 TO DATE)
12 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L28 ANSWER 25 OF 51 REGISTRY COPYRIGHT 2004 ACS on STN
RN 180509-15-3 REGISTRY
CN Phosphorofluoridic acid, (5Z,8Z,11Z,14Z)-5,8,11,14-eicosatetraenyl methyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Phosphorofluoridic acid, 5,8,11,14-eicosatetraenyl methyl ester, (all-Z)-
OTHER NAMES:
CN **Methyl arachidonyl fluorophosphonate**
FS STEREOSEARCH
MF C21 H36 F O3 P
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, CHEMCATS, TOXCENTER, USPATFULL



N-arachidonoylbenzylamine

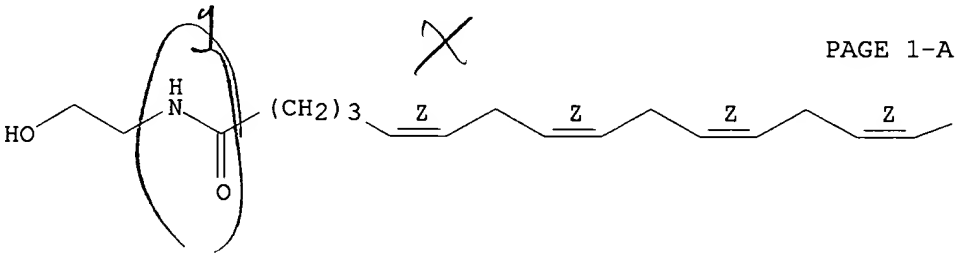


N-oleoylethanolamine

09702165

L17 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2002 ACS
RN 94421-68-8 REGISTRY
CN 5,8,11,14-Eicosatetraenamide, N-(2-hydroxyethyl)-, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 5,8,11,14-Eicosatetraenamide, N-(2-hydroxyethyl)-, (all-Z)-
OTHER NAMES:
CN Anandamide
CN **Arachidonylethanolamide**
CN N-(2-Hydroxyethyl)arachidonamide
CN N-(2-Hydroxyethyl)arachidonylamide
CN N-Arachidonylethanolamine
FS STEREOSEARCH
MF C22 H37 N O2
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CEN, CHEMCATS, CIN, CSCHEM, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, RTECS*, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

658 REFERENCES IN FILE CA (1962 TO DATE)
19 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
662 REFERENCES IN FILE CAPLUS (1962 TO DATE)

=> am 404
103222 AM
447 AMS
103660 AM
(AM OR AMS)
1691 404
L18 1 AM 404
(AM(W)404)

=> dis l18

L18 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 183718-77-6 REGISTRY
CN 5,8,11,14-Eicosatetraenamide, N-(4-hydroxyphenyl)-, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

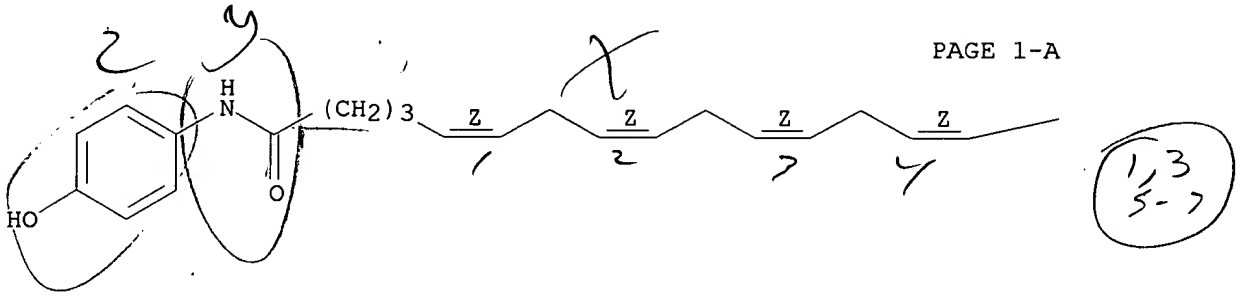
Compound of Claims 7 & 14

09702165

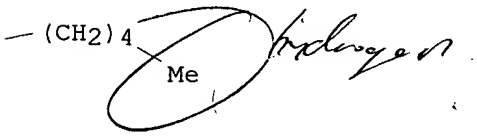
OTHER CA INDEX NAMES:
CN 5,8,11,14-Eicosatetraenamide, N-(4-hydroxyphenyl)-, (all-Z)-
OTHER NAMES:
CN **AM 404**
FS STEREOSEARCH
DR 198022-70-7
MF C26 H37 N O2
SR CA
LC STN Files: BIOSIS, BIOTECHNO, CA, CAPLUS, CHEMCATS, CSCHEM, EMBASE, TOXCENTER, USPATFULL

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 17:26:19 ON 15 JAN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 14 JAN 2004 HIGHEST RN 637725-36-1
DICTIONARY FILE UPDATES: 14 JAN 2004 HIGHEST RN 637725-36-1

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

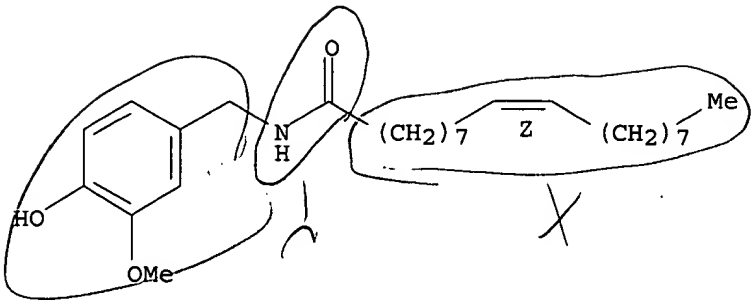
Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> olvanil/cn
L1 1 OLVANIL/CN

=> dis

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 58493-49-5 REGISTRY
CN 9-Octadecenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (9Z)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 9-Octadecenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (Z)-
OTHER NAMES:
CN N-Vanillyl oleic amide
CN N-Vanillyloleamide
CN NE 19550
CN **Olvanil**
FS STEREOSEARCH
MF C26 H43 N O3
LC STN Files: AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, CSCHEM, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSRESEARCH, IPA, MEDLINE, PHAR, PROMT, RTECS*, TOXCENTER, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

72 REFERENCES IN FILE CA (1907 TO DATE)
72 REFERENCES IN FILE CAPLUS (1907 TO DATE)